UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,350	10/11/2001	Martin J. Jacobs	CP215	9510

7590 01/11/2005

Robert T. Hrubiec
Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380

EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,350	JACOBS ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 13-15, 17-2 and 32-58* is/are rejected.

7)☐ Claim(s) *12,16 and 21-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of petition to revive application filed 11/17/03, which petition was granted 12/03/03. Examiner further acknowledges receipt of amendment, remarks and request for continued examination filed 11/17/03; and status letter filed 11/29/04. The amendment filed 11/17/03 is considered as per applicants' request and claims 1-58 are pending.

Claim Rejections - 35 USC § 112

NEW MATTER

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 55-57 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding claims 55-57 reciting "modafinil compound is the levorotatory form of modafinil," it is respectfully noted that paragraph [0026] of the published application states that "as used herein "a modafinil compound" or "modafinil compound" and the like, refers to modafinil, its racemic mixtures, individual isomers, acid addition salts, such as a metabolic acid of modafinil, benzhydrylsulfinylacetic acids, and its sulfone forms, hydroxylated forms, polymorphic forms, analogs, derivatives, cogeners and prodrugs thereof. Prodrugs are known in the art as compounds that are converted to the active agent (a modafinil compound) in the body of a subject. In certain preferred embodiments, the modafinil compound is modafinil."

Modafinil compound is not referred to as the levorotatory form. The paragraph indicates that present application has not intended to use levorotatory modafinil in the application. Therefore, the recitation that the modafinil compound is the levorotatory form is new matter.

Claim Rejections - 35 USC § 102

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-4, 6, 32, 33, 36, 37, 39, 41-44, 47, 48, 51, 52, 54 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Grebow et al. (US 5,618,845).

Grebow teaches a pharmaceutical composition comprising modafinil particles or modafinil pharmaceutically acceptable salt particles (abstract, column 2, column 3, lines 1-55 and claims 1 and 2) and non-toxic pharmaceutically acceptable carrier (column 4, lines 4-10). Grebow's composition contains an appropriate dosage of between 50 mg and 700 mg of modafinil with a preferred amount of 400 mg (column 4, lines 11-18 and column 10, lines 15-17). The modafinil pharmaceutical composition is administered as a tablet, capsule, powder, pill, liquid, suspension or emulsion; the modafinil composition can also be administered topically via epidermal patch or administered via direct injection (column 10, lines 18-26). Grebow further teaches a method of altering somnolent state, for example, narcolepsy, idiopathic hypersomnia and related sleep disorders by administering to a mammal a pharmaceutical composition comprising an effective amount of modafinil particles; and an effective amount of the pharmaceutical composition is defined as an amount effective for treating the somnolent state (column 3, lines 56-67). In human clinical trials, modafinil is administered to physically and mentally healthy male subjects (column 5, lines 46 to 56).

The composition of Grebow encompasses stable and unstable suspensions because the prior art does not exclude stable suspensions and thus the suspension of Grebow would be inherently stable. It is also noted that Grebow discloses suspensions containing modafinil and in the suspension modafinil is not crystalline and the particles of modafinil are suspended in the solvent. Grebow clearly teaches the composition and methods of the application recited in the claims designated above. Therefore, the teachings of Grebow meet the limitations of the claims.

Response to Arguments

Applicants argue that "particle forming composition" gives "life and meaning and vitality" to the claims and as such should be given patentable weight. However, applicants state that to expedite the prosecution of the application, applicants amended claim 1 to read, "said composition forms non-crystalline particles of the modafinil compound upon contact with an aqueous medium." Applicants further state that Grebow discloses various particle sizes of crystalline modafinil and that Figures 2-5 of Grebow show pictures of boulder-type crystalline structure of modafinil.

5. Applicants' arguments filed 11/17/03 have been fully considered but they are not persuasive. Grebow discloses pharmaceutical composition comprising modafanil particles in defined size and the pharmaceutical composition of Grebow is administered as a suspension or emulsion and suspensions or emulsions have particles and these particles are not necessarily crystalline or non crystalline. Specifically, Grebow does not refer to the particles as crystals and the data/Figure referred to by the applicants are scanning electron micrograph data and not X-Ray crystallographic data. It is respectfully noted that the claims are not directed to non-crystalline modafinil or non-crystalline modafainil compounds. The claims are directed to

compositions in which modafainil particle is the active ingredient in and in such a composition modafainil is not crystalline. However, claim 1 is a composition that comprises modafinil and the claim is so broad that another composition that contains modafinil would meet that limitation. A composition is characterized by having a carrier and water is an acceptable pharmaceutical carrier. It is examiner's position that when a prior art composition that contains modafinil is placed in contact with aqueous medium or contacts aqueous medium, that composition would also form non-crystalline particles as stated in claim 1.

6. Claims 1-4, 6, 7, 11, 14, 15, 32, 33, 36, 37, 39, 47, 51 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Nguyen et al. (US 5,843,347).

Nguyen teaches a pharmaceutical composition comprising particles or microparticles of active ingredient, physiologically acceptable hydrophilic excipient and water (abstract). The hydrophilic excipient comprises a polymer component and a water-soluble or water dispersible component that acts as a diluent (column 6, lines 1-5). The polymer component is selected from the group consisting of gum Arabic, xanthan gum, gum tragacanth, alginates, pectinates, polyvinylpyrrolidone, **polyethylene glycols**, cellulose, carboxymethyl cellulose, cellulose ethers, carboxymethyl chitin, dextran, chitosan, gelatin, acrylic and methacrylic polymers and copolymers, colloidal silica and mixtures thereof (column 6, lines 11-23). The water-soluble or water dispersible component is selected from the group consisting of lactose, glycocoll, mannitol, glucose, sucrose, maltodextrin, cyclodextrins and derivatives thereof (column 6, lines 44-49). The hydrophilic excipients can also comprise surfactants that are capable of oral administration and the surfactants can be polysorbates, sorbitan esters, fatty glyceride polyethers, lecithins, sodium lauryl sulfate, sodium dioctylsulfosuccinate and mixtures thereof (column 7,

lines 2-7). The process of preparing the modafinil particles involves homogenization of the active ingredient in solution, suspension, or emulsion and freeze drying or lyophilization (column 8, lines 15-24). The active ingredient is selected form the group consisting of paracetamol, probucol, piroxicam, phloroglucinol, tiadenol, flerobuterol, **modafinil**, dexfenfluramine, carbinoxamine maleate, loperamide, lorazepam and mixtures thereof (claim 13). Oral administration is route of administration and route of administration of a composition is not critical in a composition claim.

Nguyen does not exclude stable emulsion and since the prior art is silent on whether the emulsion is stable or unstable, the emulsion of the prior art would necessarily be stable since Nguyen does not teach that the emulsion is unstable and since the emulsion is homogenized and lyophilized. Nguyen does not specifically refer to polyethylene glycol as an organic solvent; but since one of the organic solvents in the application is polyethylene glycol, Nguyen teaches polyethylene glycol organic solvent. The method steps in claims 36 and 37 broadly contacts modafinil particles with water and the composition of Nguyen contains water. Thus Nguyen clearly teaches the composition and the methods of the application in the claims designated above. Therefore, the teachings of Nguyen meet the limitations of the claims.

Response to Arguments

Applicants argue that Nguyen does not disclose that the modafinil particles form non-crystalline particles in contact with water/aqueous medium and that Nguyen's preparation is pasty.

7. Applicants' arguments filed 11/17/03 have been fully considered but they are not persuasive. Both the composition of the instant claims and the composition of the prior art

contain modafinil, and modafinil is modafinil and the fate of one modafinil should be the fate of the other. What in the modafinil of the instant claims distinguishes it from the modafinil of the prior art so that the modafinil composition of the instant claims form non-crystalline particles in contact with aqueous medium and the modafinil composition of the prior art would non form non-crystalline particles in contact with aqueous medium. The claims are not directed to modafinil compounds or modafinil but to compositions.

Claim Rejections - 35 USC § 103

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 17, 18, 34, 35, 38, 45, 46, 49, 50 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grebow et al. (US 5,618,845).

The teachings of Grebow are as described above where it is noted that the appropriate dosage of modafinil is between 50 mg and 700 mg with a preferred amount of 400 mg (column 4, lines 11-18 and column 10, lines 15-17). The dose or amount of modafinil in the composition of the application recited in claims 17, 18, 34 and 35 is encompassed in the amounts disclosed by Grebow. Grebow also teaches administering the prior art composition in clinical trials to mentally and physically healthy male subjects. Orally administering modafinil particles to human subjects (column 5, lines 46-56) would necessarily bring modafinil particles in contact with the aqueous environment in the human subject since human body is mostly water.

Claim 3 of the application does not recite any dose and claims 45 and 46 depend from claim 3. But the dose/amount of modafinil administered to a subject in need thereof in the prior

art is effective for treating the somnolent state, and thus modafinil would be present and capable of detection in the blood serum of said subject because, for a drug to be effective, it has to be present in the blood circulation. In the absence of a showing to the contrary, modafinil blood serum levels of 0.05 to 30 μg/ml do not patentably distinguish the invention over the prior art.

Thus, Grebow clearly teaches the composition and methods of the application except that the prior art is silent on the form of the capsule. Since the prior art is silent on the form of the capsule, hard or soft gelatin capsule, the prior art's broad teaching of a capsule encompasses both soft gelatin capsule or hard capsule. The expected result would be a modafinil particle composition encapsulated in soft gelatin capsule or hard capsule. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to encapsulate the modafinil particle composition in hard capsule or soft gelatin capsule because the prior art broadly teaches capsules and capsules can either be soft or hard. One having ordinary skill in the art would have been motivated to encapsulate the composition of the prior art in soft gelatin capsules or hard capsules since the prior art does not exclude either form of the capsule.

10. Claims 8-10, 13, 17-20, 34, 35, 38 and 40-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Lafon (US 5,180,745).

Nguyen is discussed above. However, Nguyen fails to teach administering the composition to a subject in need thereof to treat any of the conditions recited in claim 44.

But, Lafon teaches a method of treating Parkinson's disease where the method comprises administering to a patient in need thereof a therapeutically effective amount of modafinil (claim 1). For modafinil to be effective in treating Parkinson's disease, the modafinil administered must be carried by the blood to the target areas, which implies that the level of modafinil in the

blood serum is effective for treating the Parkinson's disease. In the absence of a showing to the contrary, modafinil blood serum levels of 0.05 to 30 μg/ml do not patentably distinguish the invention over the prior art.

Parkinson's disease is one of the conditions recited in claim 44. Lafon teaches that the dose administered to humans varies form 50 mg to 1000 mg (column 1, lines 33 and 34). The dose of 200 mg and 100 mg recited in claims 34 and 35 lie within the disclosed range of 50-1000 mg.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to orally administer the composition of Nguyen to treat Parkinson's disease because Lafon administers modafinil to treat the disease. One having ordinary skill in the art would have been motivated to treat Parkinson's disease by administering to a subject in need of treatment the composition of Nguyen where the modafinil dose is 50 mg to 1000mg because Lafon teaches that the dose of modafinil administered to humans varies from 50 mg to 1000 mg.

Response to Arguments

Applicants argue that because neither Grebow nor Nguyen fails to teach formation of non-crystalline particles, the rejection under 35 USC cannot be sustained.

11. Applicants' arguments filed 11/17/03 have been fully considered but they are not persuasive because Grebow and Nguyen anticipate the designated claims as discloses compositions that contain modafinil.

12. Claims 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grebow et al. (US 5,618,845) in view of Lafon (US 4,927,855).

Grebow is discussed under 35 USC 102. Grebow also suggests that modafinil is known to be used in the art for treating Alzheimer (column 10, lines 40-44). Grebow discloses in the background section at column 1, lines 61-64, that the levorotatory form of modafinil is used to treat other diseases including Alzheimer. Grebow does not however disclose a pharmaceutical composition that comprises the levorotatory form of modafinil. But since Grebow specifically discloses that modafinil can be used to treat Alzheimer and Lafon discloses that the levorotatory form of modafinil is useful in the treatment of Alzheimer (abstract), it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the pharmaceutical composition of Grebow and use it to treat Alzheimer. One having ordinary skill in the art would have been motivated by Lafon to prepare the composition of Grebow with the levorotatory form of modafinil and use the preparation to treat Alzheimer with the expectation that as disclosed by Lafon, the levorotatory modafinil would be effective in the treatment of Alzheimer.

Double Patenting

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. Claims 1, 3-5, 14, 15, 32-35 and 44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 7, 8, 10-13, 26-29, 31 and 32 of U.S. Patent No. 6,489,363. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to pharmaceutical composition where the composition comprises modafinil compound that is modafinil. The issued claims are directed to pharmaceutical composition that comprises a modafinil compound

that is modafinil. The difference between the application and the co-pending application is that the application is directed to a particulate form of modafinil and the issued claims are silent on particulate form of the drug. However the generic teaching of modafinil in the co-pending application encompasses modafinil particles of the examined application.

Examiner thanks applicants for reminding the examiner that the copending application is issued as US 6,489,363 and in light of the issuance of the copending application as a patent, the provisional obviousness-type double patenting rejection is dropped in favor of a double patenting rejection that is now made. Applicants' argument that the issued claims do not state that the modafinil form non-crystalline particles is not persuasive because the modafinil claimed broadly is modafinil and what happens to the modafinil of the examined claims will happen to the modafinil of the issued claims except where the claimed modafinil and the issued modafinil are different are different. If they are different, then they cannot both be modafinil. But is it is respectfully noted that the issued claims and the examined claims are compositions that contain modafinil.

15. Claims 12, 16 and 21-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims because the prior art does not disclose a modafinil containing composition that has a second surfactant that is a polyoxyethylene sorbitan fatty acid ester.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600